Pancreatic Lithiasis and Calcification

A Study of 22 Cases in a Series of 35,000 Necropsies

WELDON K. BULLOCK, M.D., and HUGH A. EDMONDSON, M.D., *Los Angeles*

THE presence of calculi within the ducts of the pancreas presents problems in pathogenesis, diagnosis and treatment which are difficult to solve. During the past decade, however, much progress has been made toward that end. In this paper we shall briefly review the problem and some of the more recent contributions to our knowledge, as well as report 22 additional instances of lithiasis or diffuse calcification of the pancreas.

As pancreatic calculi arise from the juice within the ducts, the normal chemical and physiological mechanisms involved in its elaboration are of basic importance. Pancreatic juice is secreted chiefly following meals, but continuous secretion in the fasting state in man is indicated by the experiments of Agren and Lagerlof[1] and Frisk and Welin[12] to be about 12 cc. per 20 minutes. Difficulties in arriving at the true figures include the exclusion of hydrochloric acid from the duodenum and the possibility of bile entering the duodenum and stimulating pancreatic secretion during this experiment. The total 24 hour secretion of the pancreas in man may be much higher than the usually accepted figure of 700 cc., according to Miller and Wiper.[21] They studied three patients with external pancreatic fistulae. One of these produced as much as 1,770 cc. in one day. As his digestion was not disturbed and the stools were normal as to fat content, sufficient amounts of juice were probably entering the duodenum for intestinal digestion. These authors, therefore, believed the total daily secretion in man might reach 2,400 cc. Harms[16] found the pressure within the ducts of the pancreas during the height of secretion to be considerably higher than that in the common bile duct; only during fasting was it lower.

The quality of the pancreatic juice differs greatly, depending upon the stimulating agent. With vagal or pilocarpine stimulation the juice is small in quantity and high in enzyme activity. With secretin stimulation the juice is much greater in quantity, more alkaline and poor in enzymes. Komarov, Langstroth and McRae[18] in 1939 confirmed and further elaborated the work of Ball[4] in 1930 and that of Gamble and McIver[13] in 1928 regarding, first, the relationship of chloride and bicarbonate fractions to the degree of alkalinity and, secondly, the similarity of the inorganic constituents of the juice to the level of the same ions in the blood serum. In the juice of both dogs and man the inorganic ions are chiefly sodium, bicarbonate and chloride. The other ions—potassium, calcium, magnesium and phosphate—are present in much smaller quantities. Injection of sodium and potassium into the blood stream increases their content in the blood serum and pancreatic juice to the same degree. Thus it is assumed that the pancreatic acini are freely permeable to these ions. Calcium, magnesium and phosphate are secreted with much more difficulty. Ball also demonstrated in dogs that the blood serum and pancreatic juice had identical osmotic pressures. The pH of the juice increases with secretory activity. This is due to an increase in the bicarbonate fraction and a concomitant decrease in the chloride. However, the sum of the two remains constant. Ball observed during the height of secretory activity a pH of 8.24. He calculated that 8.3 was the maximum pH the pancreatic juice could reach by assuming a free CO_2 concentration of 1 millimol and a maximum bicarbonate of 150 millimols.

Most pancreatic calculi are composed chiefly of calcium carbonate and small quanities of tribasic calcium phosphate. Magnesium carbonate and calcium oxalate have occasionally been observed. Stones have also been classified into inorganic and organic types, the latter containing fat, fatty acids, carbon, cholesterol and albumin, bound together with calcium salts.[7] It has been assumed by many that because of the low concentration (1 to 1.7 millimols) of calcium in the pancreatic juice the formation of calcium carbonate calculi is difficult to explain and that additional factors such as inflammation with outpouring of more calcium might be necessary. On theoretical grounds this may be disputed if one takes into consideration the fact that the pH in the human pancreatic juice goes as high as 8 and the bicarbonate as high as 127 millimols.[3] Under these conditions the solution, even with 1 millimol of calcium present, is supersaturated.*

Pancreatic lithiasis may be symptomless or there may be a long history of upper abdominal complaints. The occurrence of solitary stones without symptoms is not unusual and their origin is only conjectural. Comfort, Gambill and Baggenstoss[10] at the Mayo Clinic in 1946 made an outstanding contribution in their study of 29 cases of primary "chronic relapsing pancreatitis." The disease is characterized by repeated attacks of upper abdominal pain, elevated serum amylase and lipase values and often temporary derangement of both the external and islet cell secretions. With repeated attacks the latter changes may become permanent and diabetes mellitus, steatorrhea and creatorrhea may be present. Stones or diffuse calcification was diagnosed in 14 of the 29 cases. Comfort and his co-workers divided these 29 patients into seven clinicopathological

From the Department of Pathology, School of Medicine of the University of Southern California, and the Laboratory of the Los Angeles County Hospital.

*Detailed calculations regarding the physical chemistry involved will be published in the future in collaboration with John W. Mehl, Ph.D.

groups, depending upon the presence of pain alone or various combinations of pain followed by one or more of the major complications: diabetes mellitus, steatorrhea or lithiasis. They believed the stones were secondary to the pancreatitis and observed the formation of calculi, while patients were under their care, within one to fourteeen years after the onset of pancreatitis. This disease is of great importance because a diagnosis can so often be made with great certainty. The exact mechanism of stone formation in the ducts of a pancreas subject to repeated attacks of inflammation is not known. Obstruction, stasis, epithelial desquamation and inflammatory exudate may all play a part in instigating the process. Alcohol probably acts only in precipitating the pancreatitis by overstimulation. Jaleski[17] noted that 45 per cent of the patients having pancreatic lithiasis reported in the literature were alcoholics. Recently Wechsler and Weimer[26] reported two younger individuals with pancreatic lithiasis whose abdominal symptoms began in childhood at the ages of eight and ten, and the calculi were diagnosed at the ages of 27 and 28. These patients were not alcoholics. It has been suggested that there is a possibility of calculi being a late complication of cystic fibrosis of the pancreas, a disease usually seen in the first two years of life.

The incidence of pancreatic lithiasis is low. In nearly all articles on the subject the total number reported in the literature is mentioned and brought up to date. The latest tabulation noted is that of Lionello, Ficarra and Ryan,[19] in which the total reported was 225. As the total number appears to be growing at a more rapid rate, its importance seems to be diminishing. The incidence in various autopsy series varies considerably. Pascucci[22] tabulated all those reported previous to 1944. There were 52 instances in a total of 117,031 routine necropsies, an incidence of 0.044 per cent.

Beling[5] in 1940 first made the suggestion that diffuse calcification of the pancreas be separated from the more common form of the disease in which there are only discrete intraductal calculi. He collected 12 instances from the literature and added one. He gives Allen[2] credit for the first reported case in 1903. Wirts and Snape[27] in 1947 collected 22 cases from the literature plus two of their own. The patients have minute calculi in the finer ducts and in the acini. The calcification is said not to involve the epithelium of the acini. Severe interlobular fibrosis and acinar atrophy are usually present. The larger ducts may be dilated and also contain minute calculi. The basis for separation of this group is that apparently the disease begins in the smaller ducts or acini and involves the entire gland, producing a stone-hard organ that can be distinguished by x-ray examination to have a separate pattern. From the clinical standpoint this group is closely similar to the larger one in which sizable calculi are in the ducts.

DIAGNOSIS

Many articles have dealt with the diagnosis of pancreatic calculi. It is agreed that a flat roentgenogram of the pancreatic area is of most importance. This should be made before any barium is present in the digestive tract or gallbladder dye studies are attempted. If shadows are present in the pancreatic area, Beling[6] emphasizes the importance of lateral films in order to bring out their relationship to the spine. The pancreas lies 1 or 2 cm. in front of the spine, although the tail may be curved and on the same plane as the body of the vertebrae. Four types of calculi have been described by Gillies.[14] The differentiation of disseminated calcification from discrete calculi depends upon the demonstration of a diffuse, stippled calcification involving the head, body and tail.[27] In addition to roentgenologic evidence of calcification in the pancreas, studies of the external secretions are of importance. A notable step in this direction was made by Agren and Lagerlof.[1] They have introduced the use of a specially designed double-lumened tube, to be introduced into the stomach and duodenum, which aspirates both gastric and duodenal secretions at the same time. With secretin injection intravenously there is a prompt increase in the volume of the pancreatic juice and especially an increase in bicarbonate and enzymes. In both chronic pancreatitis and stone, marked reduction in volume, alkalinity and enzymes may be observed.[9] In recurrent attacks of pain associated with chronic pancreatic disease with or without calculi, studies of serum amylase and lipase[10] are most helpful. It is to be remembered that in long-standing obstruction by stone in the head of the pancreas coincidental with acinar atrophy the levels of amylase and lipase tend to decrease in recurrent attacks of pancreatitis. Other laboratory aids to diagnosis are well known and no particularly new developments have been noted. These include examination of the stools for fat and the percentages of neutral fat and fatty acids, tests for glycosuria and glucose tolerance tests.

REPORT OF CASES

There were 22 instances of pancreatic lithiasis and/or calcification among 35,000 consecutive autopsies performed between September 15, 1925, and August 19, 1947. They were evenly divided as to sex. The range of age was from 22 to 86 years, the mean age for the entire group being 53.4 years. The males were considerably older, the mean being 64.1 as against 43.6 for the females. Death was attributable directly to chronic pancreatitis and lithiasis in seven cases, and the disease was contributory in six. In the remaining nine instances the pancreatic disease was not a direct factor in the cause of death.

Clinical:

The symptoms and signs of the disease were not definitive. The following were noted at the time of the admission of the patients to the hospital.

Symptoms		Signs	
Upper abdominal pain	10	Weight loss	17
Weakness	8	Hepatic enlargement	11
Nausea and vomiting	8	Jaundice	5*
Constipation	6	Edema	1
Diabetes (thirst, polyuria or coma)	6	Ascites	1
Steatorrhea	1		

*In addition the examining doctors later noted icterus in nine additional cases, making a total of 14.

The chief presenting symptom was upper abdominal pain of some kind. No two patients complained of exactly the same symptoms. In some the pain was of a severe colicky nature, while in others it was a vague distress. Radiation of the pain was likewise of little assistance in making a diagnosis. Sometimes it would radiate to the right upper quadrant, other times through to the mid-portion of the back. The pain seldom resembled that of biliary colic. One of the patients had pain in both flanks and was thought to have an acute pyelonephritis. The pain of pancreatic lithiasis is often associated with nausea and vomiting, but the two do not necessarily go together.

The other symptoms and signs noted by the patients, such as weakness, loss of weight and constipation, are of no help in arriving at a correct diagnosis. Steatorrhea occurred but once in this series; other forms of diarrhea were absent. Diabetes mellitus occurred in seven instances, and in six instances it was the primary reason for the patient's entry to the hospital. In one patient the disease was latent, being diagnosed by the glucose tolerance test. Four patients did not complain of pain. One was known to have had diabetes for three years, which had been controlled by diet until two days previous to final entry into the hospital. Jaundice was an outstanding sign in 14 instances, although only five patients noticed the icterus. The diagnosis of chronic pancreatitis with lithiasis was not made clinically in any of the 22 cases. A specimen taken of the head of the pancreas in one patient operated upon for obstructive jaundice resulted in a report of chronic interstitial pancreatitis. At necropsy this was confirmed but the underlying cause was intraductal calculi.

There was a definite history of long use of alcohol in ten instances. In two the matter was questionable, and in ten cases there was no notation of intake of alcohol.

The histories of two of the patients are of particular interest. One of these had obstructive jaundic due to pressure on the common duct and the case was reported in detail at the Clinical-Pathological Conference of the California Medical Association on May 3, 1947, by Dr. John Tragerman (published in CALIFORNIA MEDICINE, 67:256-258, October, 1947). The second case is as follows:

CASE REPORT

A white male mechanic, age 45, first came to the outpatient department on May 3, 1934, complaining of "bloating of the abdomen," a condition that had existed for 18 years. This would often cause so much distress that nausea and vomiting would result, with subsequent relief. No true abdominal pain was associated. Soda gave no relief. The attacks would last from one to five days and would recur every six to twelve months. For one year the patient's appetite had been poor and he had lost 15 pounds in weight. He used alcohol, but the history does not state in what quantities. On May 9 barium study revealed an irregular, tender duodenal cap. A diagnosis of duodenal ulcer was made. The patient returned to the outpatient department in June and July of 1934 complaining only of severe upper abdominal pain. He entered the hospital on August 13, 1935, complaining of similar pain but refused treatment and was discharged. He reentered the hospital September 2, 1935, from another hospital in a moribund condition and died a few hours later. At necropsy no evidence of a duodenal ulcer was identified. The cause of death was a solitary stone in the duct of Wirsung with a complicating acute pancreatitis.

This history illustrates the difficulty in differential diagnosis between pancreatic calculi and duodenal ulcer.

Pathology:

Study of specimens in this series revealed only the end stages of obstructive disease of the pancreatic duct and therefore tells us very little of the genesis of the calculi.

Gross Pathology: The descriptions of the pancreases in gross are of interest chiefly from the standpoint of the location of the calculi and their complications. In nine cases calculi were within 2.5 cm. of the ampulla Vater. In two of these cases the calculi had obstructed the common duct, apparently by pressure and edema, which resulted in jaundice in both patients and biliary cirrhosis in one. Of particular interest was a large ivory-like stone which obstructed the duct of Wirsung in the head of the pancreas, but there was little dilatation or change in the duct system behind the obstruction. This brings up a point which apears to have been omitted in most published discussions of pancreatic calculi; that is, whether or not the communicating duct of Santorini may carry the pancreatic secretions to the duodenum when the duct of Wirsung is blocked. In ten patients the calculi were in the body or tail, or were described as being widespread in the duct system but no definite location was given. There were three instances of diffuse calcification of the pancreas, so-called petrificans, without stones in the duct. Of the entire group of patients, 16 had multiple calculi or calcification, and in six there was a solitary stone within the duct. Seven had one or more cysts somewhere in the pancreas. Some of these were apparently dilatations of ducts and others were pseudocysts. The complications were what one would expect with obstruction of the duct: three had acute pancreatic necrosis; two, healing fat necrosis; in four there was evidence of purulent inflammation, with solitary abscesses having resulted in two of them.

Microscopic Pathology: The microscopic changes were of interest because of the variations in degree of dilatation of the duct and fibrosis of the pancreas. With apparently similar degrees of gross obstruction there was great variation in microscopic evidence of dilatation. This again emphasizes the possibility of some of the pancreatic juice escaping through the duct of Santorini. Regardless of the degree of dilatation of the duct, dilatation of the acini was minimal or even absent. Rich[24] has proven that with increased pressure within the ducts fluid easily escapes between the acinar cells into the peripancreatic tissue. Diffuse perilobular and intralobular fibrosis were common, but atrophy alone appeared to have occurred in some instances, leaving little evidence of chronic inflammation and fibrosis. In some of those patients with solitary calculi, dilatation and atrophy alone were observed. The question of what role

repeated attacks of pancreatitis have in the formation of fibrous tissue arises but cannot be solved from this material. Islets apparently are not always, as has been taught, spared until the last. One of the patients had diabetes mellitus without great acinar atrophy or evidence of steatorrhea.

Associated Pathology: There were 14 in whom the liver was fatty. Eleven of these had cirrhosis. In eight it was Laennec's type; in two it was biliary cirrhosis due to obstruction of the common duct by a stone in the duct of Wirsung; and in one the cirrhosis was of the fatty dietary type with no particular relationship to periportal spaces or central veins—a condition similar to that described by Chaikoff[8] in experimental dietary fatty cirrhosis of animals.

COMMENT

It seems strange that in such a large series as this not a single correct diagnosis was made antemortem in spite of the fact that many of the known symptoms of pancreatic calculi were present. Because pancreatic disease was not suspected, laboratory procedures useful in diagnosis were not performed. One patient had a roentgengram of the pancreatic area which showed calcification but this was interpreted as an artifact. The incidence of the disease in this necropsy series, 0.062 per cent, is somewhat higher than the general average of 0.044 per cent reported by Pascucci.[22] Six of the 22 patients in our series were seen within the year preceding the preparation of this paper. All were chronic alcoholics. During the same period calculi was diagnosed in a patient on the wards and we were consulted about another case by one of our colleagues. Thus, having seen or known of eight instances of the disease in one year, we feel that it hardly belongs among the rare diseases. Taking into consideration the present consumption of alcohol and the number of chronic alcoholics in the population, an increase in incidence of pancreatic lithiasis might be expected. The incidence in this series is probably much too low, as often the pancreatic ducts were not dissected at autopsy. At present we are examining a series by postmortem roentgenograms to compare with Ludin's[20] series in Basel. Ludin carefully dissected all pancreases showing calcific roentgenographic shadows and found 28 stones in 542 pancreases, giving an incidence of 5.1 per cent.

The complications of lithiasis in this series are similar to those that have been reported. Among the local disturbances within the pancreas are atrophy, acute pancreatitis, abscesses and pseudocysts. Many of the stones were probably due to recurrent attacks of pancreatitis of the type described by Comfort.[10] In patients with symptomless solitary stones in whom no evidence of chronic inflammation was noted, other explanations for the formation of calculi should be considered. In four of the six patients with solitary calculi no symptoms attributable to the pancreas were elicited. It is possible, of course, that a minimal attack of pancreatitis forgotten by the patient could give rise to a stone.

Complications arising from pressure on contiguous structures, especially the common duct and duodenum, should be remembered. Additional pressure phenomena mentioned by Comfort[10] include pressure on the splenic vein and mesenteric vessels.

Perhaps the pathological physiological sequelae are the most interesting of all. These include diabetes mellitus, steatorrhea and fatty metamorphosis of the liver with or without cirrhosis. Increase in serum amylase and lipase may occur in the recurrent attacks of pancreatitis which often characterize the disease. Any of these, when present, constitute important leads to correct diagnosis. Flat films of the pancreatic region are now being requested on all patients entering the hospital in an acute attack of pancreatitis. It may be questionable from the economic standpoint whether the same procedure should be done on all diabetic persons. Seven, or 31.8 per cent, of the 22 patients in this series were diabetics. From the histological study of these it appears that occasionally the atrophy of the islets and acini proceeds at a parallel rate and the islets are not preserved until the last. In Comfort's[10] series of 29 there were four patients who had upper abdominal pain followed by diabetes and calcification, but there was no evidence of steatorrhea. Two causes for this may be mentioned: First, the calculi or calcification may involve primarily the body and tail, where most of the islets are present; even though there were great destruction here, the acinar tissue in the head of the pancreas might produce sufficient external secretion to prevent steatorrhea. Second, once islet tissue is partially destroyed, episodes of hyperglycemia may produce progressive damage to the islets alone, the effect being somewhat similar to that seen in experimental animals, both normal and partially depancreatized, in which prolonged intraperitoneal glucose-saline solution with hyperglycemia produced permanent damage to the islets.[11] The low incidence of steatorrhea (one in twenty-two) probably means that the stools were not examined carefully. The fatty change noted in the liver with or without cirrhosis was in every instance associated with chronic alcoholism.

The treatment of pancreatic lithiasis, when possible, is surgical.[15, 25] Discussion of this subject is beyond the scope of this paper. Haggard and Kirtley state that the results are good following the removal of stones. Early diagnosis and surgical treatment are emphasized by most authors. The importance of control of pain by sympathectomy and vagotomy has recently been introduced by Reinhoff and Baker.[23]

SUMMARY

1. Twenty-two instances of pancreatic calculi and/or calcification in a series of 35,000 necropsies are reported.

2. In 14 of these there were multiple calculi; in five they were solitary. Stones lodge most commonly in the first 3 cm. of the duct of Wirsung.

3. Calcinosis or diffuse calcification were present in four cases, and in three of these four there were no grossly detectable intraductal calculi.

4. Dilatation of the ducts, atrophy of the parenchyma, fibrosis and chronic inflammation occurred to a varying degree.

5. Fatal complications included acute pancreatitis, suppuration of the pancreas, and obstruction of the common bile duct.

6. Atrophy of acini and of islets may occasionally proceed at a more parallel rate than is usually recognized. Diabetes mellitus was present in seven patients in this series.

7. The signs and symptoms of the disease in this series were difficult of evaluation. Not a single case was diagnosed correctly.

8. The most important diagnostic aid is roentgenograms of the pancreas.

9. Alcoholism and recurrent pancreatitis resulting in fibrosis are common precursors of calculi and calcification. Ten in this series were chronic alcoholics.

10. Pain, weight loss, jaundice, and a palpable liver were the predominating clinical manifestations.

11. The disease may be symptomless.

REFERENCES

1. Agren, G., and Lagerlöf, H.: The pancreatic secretion in man after intravenous administration of secretin, Acta Med. Scand., 90:1-29, 1936.

2. Allen, L. W.: Chronic interlobular pancreatitis with pancreatic calculi, Ann. Surg., 37:740, 1903.

3. Babkin, B. P.: Secretory mechanism of the digestive glands, p. 738, Paul B. Hoeber, Inc., New York, 1944.

4. Ball, Eric G.: The composition of pancreatic juice and blood serum as influenced by the injection of acid and base, J. Biol. Chem., 86:433 (April), 1930; The composition of pancreatic juice and blood serum as influenced by the injection of inorganic salts, J. Biol. Chem., 86:449 (April), 1930.

5. Beling, C. Abbott: Calcification of the pancreas, Am. J. Digest. Dis., 7:231 (June), 1940.

6. Beling, C. Abbott, Baker, Charles Frederick, and Marquis, W. James: Pancreatic calcification, Radiology, 38:188 (Feb.), 1942.

7. Bosq, P.: Pancreatolithiasis, Rev. sud-am. de endrocrinol., 18:475 (July), 1935.

8. Chaikoff, I. L., Eichorn, K. B., Connor, C. L., and Entenman, C.: The production of cirrhosis in the liver of the normal dog by prolonged feeding of a high-fat diet, Am. J. Path., 19:9 (Jan.), 1943.

9. Comfort, Mandred W., and Osterberg, A. E.: The value of determination of the concentration of serum amylase and serum lipase in the diagnosis of disease of the pancreas, Proc. Staff Meet., Mayo Clin., 24:1137 (July), 1940.

10. Comfort, Mandred W., Gambill, Earl E., and Baggenstoss, Archie H.: Chronic relapsing pancreatitis. A study of twenty-nine cases without associated disease of the biliary or gastro-intestinal tract, Gastroenterology, 6:239 (April), 1946.

11. Dohan, F. C., and Lukens, E. D. W.: Lesions of the pancreatic islets produced in cats by administration of glucose, Science, 105:183 (Feb. 14), 1947.

12. Frisk, A. R., and Welin, G.: The external pancreatic secretion and the discharge of bile during hypoglycemia following intravenous administration of insulin, Acta Med. Scand., 91:170-182, 1937.

13. Gamble, J. L., and McIver, M. A.: (b) Acid-base composition of pancreatic juice and bile, J. Exp. Med., 48:849 (Dec.), 1928.

14. Gillies, C. L.: Pancreatic lithiasis with report of a case, Am. J. Roentgenol., 41:42 (Jan.), 1939.

15. Haggard, William D., and Kirtley, James A.: Pancreatic calculi, Ann. Surg., 109:809 (May), 1939.

16. Harms, E.: Über druckmessungen im gallen— und pankreasgangsystem, Arch. f. klin. Chir., 147:637, 1927.

17. Jaleski, T. C.: Pancreatic lithiasis, Ann. Int. Med., 20:940 (June), 1944.

18. Komarov, S. A., Langstroth, G. O., and McRae, D. R.: The secretion of crystalloids and protein material by the pancreas in response to secretin administration, Canad. J. Research, D, 17:113 (May), 1939.

19. Lionello, Joseph, Ficarra, Bernard J., and Ryan, Nicholas H.: Pancreatic calculi, Arch. Surg., 48:137 (Feb.), 1944.

20. Lüdin, M.: Die röntgendiagnostik bei pankreasaffektionen, Arch. f. Verdauungskr., 63:273, 1938.

21. Miller, Joseph M., and Wiper, Thomas B.: Physiologic observations on patients with external pancreatic fistula, Ann. Surg., 120:52-59 (July), 1944.

22. Pascucci, Lucien M.: Pancreatic cyst and lithiasis, Am. J. Roentgenol, 52:80 (July), 1944.

23. Reinhoff, William Francis, and Baker, Benjamin M.: Pancreolithiasis and chronic pancreatitis, J.A.M.A., 134:20, 1947.

24. Rich, A. R., and Duff, G. L.: Experimental and pathological studies on the pathogenesis of acute hemorrhagic pancreatitis, Bull. Johns Hopkins Hosp., 58:212 (March), 1936.

25. Seeger, S. J.: Pancreatic lithiasis, Surg., Gynec. & Obst., 40:841 (June), 1925.

26. Wechsler, Harry F., and Weimer, James I.: Pancreatic lithiasis. A report of two cases in young adults, Gastroenterology, 5:181 (Sept.), 1945.

27. Wirts, C. Wilmer, Jr., and Snape, William J.: Disseminated calcification of the pancreas: Subacute and chronic pancreatitis, Am. J. M. Sc., 213:290 (March), 1947.